Peer review file

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Reviewer A

The topic is interesting and the study is well designed. However, several issues should be raised. Results should be confirmed by the propensity score matching (considering the different number consistrency of the tw subgroups). A paragraph should be added on the potential clinical implications of serial measurements of SIRT2.

Reply:

Thank you so much for your helpful comment and suggestions. In our study, all participants were consecutively enrolled in six months, and different number of the two subgroups were included at the end of enrollment. We are not sure how to do the propensity score matching. As suggested, we added the potential clinical implications of SIRT2. Please find the relevant modifications in our revised Manuscript (Page 7, line 8-15).

Reviewer B

This study assessed the relationship between plasma SIRT2 level and AMI, and also investigated the association of plasma SIRT2 level with major adverse cardiovascular events (MACE) and heart failure after AMI. The present study suggested that plasma SIRT2 level is a promising biomarker to predict heart failure and MACE after AMI.

The author's manuscripts are actual and clinically relevant. However, several issues should be considered to assess the results in this paper.

My comments are related to the following points:
1) As the authors show there are many known, and readily available parameters that predict remodeling and recovery. The robustness of the relationship of a purported marker of risk and clinical events is highly dependent on the number of events as well as the adjustment for known prognostic factors. The question is, does SIRT2 add predictive value to these clinical parameters, such as infarct location, biomarkers, duration of occlusion, heart failure class, etc?

Reply:

Thank you so much for your helpful comment and suggestions. It is a really smart idea to evaluate the predictive value of SIRT2 for infarct location, biomarkers, duration of occlusion, heart failure class. However, for the small sample size, it is not easy to do such work in the present study. We will try it in our further study.

2) With any novel biomarker, the assessment of cut points used requires prespecified definitions or carefully defined exploratory discriminatory analyses. The authors have confined their analysis to above and below the 75th percentile value. Was the "above and below the 75th percentile value" determination a post hoc finding? Can they provide further support for the concept with linear analysis or by using other cutpoints?

Reply:

Thank you so much for your professional comment. Indeed, the "above and below the 75th percentile value" determination was a post hoc finding. Moreover, as a continuous variable, SIRT2 was also showed significant associations with MACE and heart failure. However, our study included a small sample size, and further large sample size studies are needed to determine the cutpoint.

3) It may be worth noting that plasma BNP level is one of the most important independent predictors of clinical outcomes and heart failure after AMI. However, the authors did not discuss the relationship between SIRT2 and BNP. So even if plasma BNP level was not a predictor in this study, please discuss why it was not predictor.

Reply:

Thank you so much for the detailed comments. In the present study, Univariate Cox regression analysis showed that BNP was a predictors of clinical outcomes and heart failure after AMI. However, after including GRACE and SYNTAX scores, gender, BMI, diabetes, plasma SIRT2 level, BNP>500ng/L, as well as utilization of IABP and breathing machine in the multivariate Cox regression analysis, BNP was not statistically significant for predicting clinical outcomes. The effect of BNP may be corrected by GRACE and SYNTAX scores, as well as utilization of IABP and breathing machine.

Reviewer A

Summary:
This is a single center, prospective, observational study which is assessed the relationship between elevated plasma Sirtuin2 level and clinical parameters, biomarkers and clinical outcomes after AMI. Patients were divided into two groups according to the 75th percentile value of plasma Sirtuin2 level. In total, 129 patients with AMI were enrolled and MACE which is a composite of cardiac death, readmission for revascularization and heart failure occurred in 22 patients. Multivariate regression analysis showed that there were higher risks of MACE (hazard ratio (HR)=11.20 [95%CI:3.18-39.52, P<0.001]) and heart failure (HR=27.10

[95%CI:4.65-157.83, P<0.001]) in the high level group.

There are some comments from this reviewer.

For multivariate regression analysis, authors included 10 variables which were derived from univariate analyses. However, due to small sample size (N=129) and low incidences of MACE (only 22 patients), this analysis were overstretched "rule of 10". Did authors calculate sample size?

Reply:

Thank you so much for your professional comment. We included 9 variables (GRACE and SYNTAX scores, gender, BMI, diabetes, plasma SIRT2 level, BNP>500ng/L, as well as utilization of IABP and breathing machine) in the multivariate Cox regression analysis. For there was no relevant study, we did not have the data to calculate sample size, and all the subjects in the present study were consecutively enrolled in six months.

MACE is defined as a composite of cardiac death, readmission for revascularization and heart failure. However, the incidence of cardiac death, readmission for revascularization and heart failure were not provided in the result table. Please provide them.

Reply:

Thank you so much for your helpful comment and suggestions. As suggested, we revised the related part. Please find the relevant modifications in our revised Manuscript (Page 6, line12-15).

Page 4, line19
In the text, “no death happened within 12 months”
According to the table 2, there were 6 deaths. Please clarify.

Reply:

Thank you so much for the detailed comments. We are very sorry for the wrong expression, and we want to report some deaths were during hospitalization, and some deaths were within the 12 months followed-up. Please find the relevant modifications in our revised Manuscript (Page 4, line19).

Page 7, line 20
In the text, “ the higher plasma SIRT2 level was associated with poorer AMI prognosis, especially for worse cardiac function.”
Decreased LVEF was not associated with MACE after multivariate analysis. This statement is not supported by current study.

Reply:

Thank you so much for the detailed comments. In the present study, Univariate Cox regression analysis showed that Decreased LVEF was associated with MACE. And Decreased LVEF was not included in the multivariate Cox regression analysis.